The Placebo Effect in Pain Reduction: The Influence of Conditioning Experiences and Response Expectancies

Peter J. de Jong, Robert van Baast, Arnoud Arntz, and Harald Merckelbach

We investigated the role of conditioning experiences and response expectancies in the generation of placebo effects. On 3 sequential days (Test 1, Experimental Session, Test 2), 66 female undergraduates were presented with a series of pain stimuli. For the experimental group, placebo administration (analgesic cream) was paired with a decrease in the painful stimulus. Two control groups were used to explore the relative contributions of verbally induced expectancies and contingent unconditional stimulus experiences per se. The results show that placebo-induced pain reduction can be obtained as a result of a conditioning procedure, independent of verbally induced expectancies. Mere verbal persuasion was not sufficient to elicit placebo-induced pain reduction. Irrespective of the experimental manipulations, the placebo effect was related to both reduced pain expectations and reduced fear of pain. Although conditioned placebo responses were evident at the subjective level, no placebo effects emerged at the physiological level.

Key words: placebo, conditioning, pain, skin conductance, expectations, fear

Placebo effects refer to improvements in a therapeutic context that cannot be ascribed, according to a certain theory, to specific therapeutic factors. Clinically relevant responses to inert substances (i.e., placebos) are a specific type of the placebo effect. The potential powerful effects of placebos are widely recognized.

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However, although placebos are often used in clinical practice, they still have an aura of quackery (e.g., Wall, 1992). Perhaps the most important reason for this is the ignorance of the underlying mechanisms, which prevents placebo effects from being reliably predicted and controlled.

A promising hypothesis that has been advanced to explain placebo responses is the classical conditioning model outlined by Wickramasekera (1980). In this model, the placebo effect is considered to be a conditioned response. That is, as a result of repeated pairing with an active ingredient (unconditioned stimulus [UCS]); e.g., an analgesic cream), an initially inert stimulus (conditioned stimulus [CS]) may acquire the ability to induce the same specific response (conditioned response [CR]) as the UCS (e.g., analgesia). Explaining the placebo effect in terms of classical conditioning implies that the phenomenon is the result of a systematic learning process and can be expected in any treatment situation providing that an active ingredient (UCS) is present. Most important, defining the placebo response as a CR allows for specific predictions that can be inferred from the extensive conditioning literature. Eventually, such an approach may provide us with the ability to systematically manipulate the placebo response to maximize treatment effects.

Several animal studies support the conditioning view of the placebo effect (e.g., Hernstein, 1962). Recently, Voudouris and colleagues performed a series of studies to test the validity of the conditioning model in human participants (i.e., Voudouris, Peck, & Coleman, 1985, 1989, 1990). Their studies essentially consisted of three stages: a pretest, a conditioning manipulation, and a posttest. During the pre- and posttests (on placebo as well as on no-placebo trials), all participants received pain stimulation equivalent to participants' 50-mm position on a visual analogue scale (VAS) ranging from 0 (no pain) to 100 (extreme pain). During the conditioning manipulation, half of the participants (conditioning group) received pain stimulation on a lowered level (i.e., 25 mm) contingent with the placebo cream (i.e., simulating cream-induced analgesia). The other half of the participants received pain stimuli at the original level equivalent to 50-mm VAS on all trials. Voudouris et al. (1990) found that application of the placebo at the posttest resulted in lower pain experiences for the conditioning than for the no-conditioning group. On basis of this result, they concluded that placebo responses can be conditioned in the laboratory. Given the potentially important implications of these results, this study was carried out to replicate and extend the findings of Voudouris et al. (1990).

Employing a paradigm similar to that of Voudouris et al. (1990), this study further investigated the influence of conditioning experiences and response expectancies on the placebo effect. Interestingly, several authors have argued that response expectancies play a crucial role in placebo effects (e.g., Kirsch, 1985, 1991). From this view, the effectiveness of a conditioning manipulation in evoking placebo responses is due to its power to lower pain predictions for placebo trials. Such an expectancy framework also offers a meager explanation for the finding of Voudouris et al. (1990) that a conditioning manipulation is superior to verbal
persuasion in evoking placebo responses (cf. de Jong & Arntz, 1993). That is, it might well be that a conditioning procedure is more effective in lowering pain predictions on placebo trials than verbal persuasion. Such a conceptualization also fits with recent cognitive models on human conditioning (e.g., Davey, 1987). These models emphasize that the CS (e.g., placebo cream) is a predictor of the UCS (e.g., lowered pain stimulation). This study examined the alleged mediating role of expectations. Therefore, participants were asked to report not only the experienced pain intensity on each trial but also the expected pain intensity of the next stimulus. In line with the study of Voudouris et al. (1990), participants in the experimental group received pain stimulation at a lowered level contingent with the placebo cream. To explore the relative contributions of verbally induced expectancies and UCS experiences per se, two control groups were added to the conditioning group: a verbal expectancy group and a control group that was (correctly) informed that the (electrical) pain stimulation was halved during the cream trials.

An additional issue that was explored concerns the role of (reduced) anxiety on placebo effects. Anxiety about pain might lead to the direction of attention to the painful sensations, and several studies have shown that attentional focus on pain results in stronger pain experiences (e.g., Arntz & de Jong, 1993). Accordingly, reduced fear might be one of the factors underlying placebo phenomena.

Thus far, studies on conditioned placebo responses in humans exclusively relied on self-report measures. As it would be important to know whether similar effects can be obtained at the physiological level, we also measured skin conductance responses (SCR) to the painful stimuli (as an index of autonomic reactivity). At the same time, if placebo effects could be demonstrated at the physiological level, this would reduce the possibility that the effects were induced by experimental demand.

**METHOD**

**Participants**

Participants were 66 female undergraduate students (mean age = 21.3 years). They participated voluntarily and received a small remuneration.

**Apparatus**

The electrical pain stimulation was produced by a Siemens Eltron D-413 via Beckman Ag–AgCl electrodes (8 mm; 50-mm distance between the centers of electrodes). The electrodes were attached to the lateral side of the participant's upper arm (dominant side) and were filled with Hewlett-Packard Redux Cre
The intensity of stimulation could be increased by steps of .01 mA (range = 0 mA to 40 mA).

SCR were measured via two Beckman Ag–AgCl electrodes (8-mm diameter) placed on the medial phalanges of the third and fourth fingers of the nondominant hand (the skin was cleaned with distilled water). To minimize electrical noise in SCR recording, a ground electrode was attached to the dorsal side of the participant’s nondominant hand. Electrodes were filled with an isotonic paste following the recommendations of Fowles et al. (1981) and connected to a Beckman skin conductance coupler (Type 9844). The coupler allowed for a maximum sensitivity of 0.05 microSiemens. SCR were monitored on a Beckman R711 polygraph.

Materials

To measure predicted pain, fear of the next pain stimulus, and experienced pain, 100-mm VASs were used ranging from 0 (no pain at all/no fear at all) to 100 (maximum pain/maximum fear).

The placebo analgesic was in the form of a cream (e.g., Voudouris et al., 1989). A simple cream (Unguentum Leniens; 100 gr.) was mixed with Rosal Altheroleum (10 dr.) and eosine (0.6 gr.) resulting in a cream with a distinct smell and color (pink). The experimenter was aware of the fact that the cream was in fact a placebo.

Experimental Design

The experimental design is schematically outlined in Table 1. All participants attended three sessions on 3 consecutive days. For each participant, the three sessions were held at the same time of the day to control for potential fluctuations in pain experience due to circadian rhythms. Before participants attended the first session, they were randomly assigned to the experimental group (EXP group; n = 36) or to one of two control groups. Participants in the EXP group were said that an active cream would be used, and during the experimental session the intensity of the noxious stimulation was halved during the cream trials. One control group (CO1 group; n = 14) was included to investigate the influence of contingent reduction of noxious stimulation per se. They were said that an inactive cream would be used. During all sessions, the CO1 group received similar noxious stimulation as the EXP group; however, during the experimental session, they were explicitly informed that the intensity of the noxious stimulation would be halved during the cream trials. The other control group (CO2 group; n = 16) was included to investigate the influence of verbal expectancies per se. That is, participants were informed that an active cream would be used. Yet, in contrast to the EXP and CO1 groups, there was no contingent reduction of the noxious stimulation during the
<table>
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<th>Table 1: Experimental Design</th>
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<tr>
<th>Experimental group&lt;sup&gt;d&lt;/sup&gt;</th>
<th>Assessment relationship pain-stimulation (mA) and self-reported pain (VAS: 0–100)</th>
<th>During C trials, pain stimulation halved.</th>
<th>Participants informed that pain stimulation is equal for both C and no-C trials.</th>
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<tr>
<td>Control group 1&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Assessment relationship pain-stimulation (mA) and self-reported pain (VAS: 0–100)</td>
<td>During C trials, pain stimulation halved.</td>
<td>Subjects explicitly informed that pain stimulation is halved during C trials.</td>
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<tr>
<td>Control group 2&lt;sup&gt;f&lt;/sup&gt;</td>
<td>Assessment relationship pain-stimulation (mA) and self-reported pain (VAS: 0–10)</td>
<td>Equal pain stimulation during C and no-C trials.</td>
<td>Participants informed that pain stimulation is equal for both C and no-C trials.</td>
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**Note.** C = cream; NC = no cream; mA = intensity of noxious stimulation; VAS = Visual Analogue Scale.

<sup>a</sup>Only NC trials. <sup>b</sup>10 C and 10 NC trials. <sup>c</sup>5 C and 5 NC trials. <sup>d</sup>n = 36. <sup>e</sup>n = 14. <sup>f</sup>n = 16.

Second session for the CO2 group. In sum, there were three groups: (a) EXP: contingent reduction noxious stimulation (cream is said to be active); (b) CO1: contingent reduction noxious stimulation (cream is said to be inactive); and (c) CO2: no (contingent) reduction noxious stimulation (cream is said to be active).

On Day 1 (pretest), the relation between the intensity of noxious stimulation (mA) and self-reported pain experience (VAS) was assessed. In contrast to the design of Voudouris et al. (1990), no cream was used during the first session to avoid learning experiences opposed to the conditioning manipulation (i.e., several studies have shown that isolated CS presentations inhibit subsequent learning of CS–UCS associations; this phenomenon is known as latent inhibition; e.g., Siddle & Remington, 1987).

On Day 2 (experimental session), half of the pain stimuli were presented while a cream (placebo) was applied. EXP and CO2 groups were told that the cream would lead to a temporary localized analgesia. In contrast, the CO1 group was informed that during half of the trials, a neutral (inactive) cream would be used. CO2 and EXP groups were told that electrical pain stimulation of the same intensity would
be used during both cream and no-cream trials. In fact, for the EXP group, shock intensity was halved during cream trials. The CO1 group was (correctly) informed that during cream trials, pain stimulation would be reduced to half the intensity of the no-cream trials.

The third session (posttest) was identical for all groups. Again, cream was used during half of the trials. For all groups, participants were (correctly) informed that the intensity of the electrical pain stimulation would be equal during all trials. During the experimental session as well as during the posttest, the order of cream and no-cream trials was balanced across participants, resulting for each group in four different orders (e.g., $C-NC_{session2}-C-NC_{session3}$; $C-NC_{session2}-NC-C_{session3}$; etc).

Procedure

Pretest. The first session was equal for all participants. Participants were told that the aim of this session was to assess participants' range and sensitivity to painful stimuli and that this information was pertinent for the remaining two sessions. Following this, it was stressed that the participants should very carefully rate the experienced pain during the forthcoming trials. When both electrodes were attached to the participants' upper arm, pain threshold and pain tolerance were determined by means of a shock work-up procedure. The electrical stimulation started with the 0.5 mA level and was gradually increased with small steps (.2 mA) until participants reported a judgment of 95 mm or greater. For each level, the duration of electrical stimulation was always 1 sec; interstimulus interval (ISI) was 10 sec. After the pain threshold (5 mm) and the pain tolerance (95 mm) were established, a set of 15 painful stimuli were chosen within each participants' range and were administered in a randomized order. Participants were instructed to carefully rate the painfullness of each of these stimuli. For each participant, the results of the randomized pain stimulation trials were used to determine the (approximate) relation between objective pain stimulation and self-reported pain. The objective intensity levels most closely corresponding to 25-mm and 50-mm VAS judgments were determined for use during the experimental session and the posttest.

Experimental session. First, SCR and pain stimulation electrodes were attached. Then, standardized instructions were provided by means of a tape recorder. EXP and CO2 groups were informed that (a) during this session, for half of the trials, an analgesic cream would be applied and (b) this cream would lead to a temporarily localized analgesia. The CO1 group was also told that a cream would be used on half of the trials. However, this group was (correctly) informed that on the cream trials, the intensity of the electrical pain stimulation would be halved.

After the instruction, two reference stimuli were administered corresponding to participants' 5-mm and 95-mm pain judgments (anchor points) during the first
session to increase the intersession reliability. Then, four blocks of five pain stimuli were administered. The ISI within each block was always 20 sec. During the 20-sec interval, participants rated the VASs. (Before each block of trials, participants were asked to rate the expected pain and the fear of the next stimulus.) Between each block of trials, there was a break of 5 min to allow time for applying (removing) the cream and for the cream to take effect (or for its effect to wear off). The cream was applied by means of a piece of wadding on the place where the electrical stimulation was administered. After the cream trials, the cream was removed by means of a piece of wadding soaked in chloorthexidine. Electrodes were removed during applying as well as during removing the placebo cream.

For all groups, the intensity during the no-cream trials was set at a level corresponding to participants’ 50-mm pretest VAS ratings. For EXP and CO1 groups, the intensity of the noxious stimulation on the cream trials was reduced to the 25-mm VAS level. Only for the CO2 group was the intensity of pain stimulation equal for the cream and the no-cream trials (i.e., 50-mm VAS level).

**Posttest.** As in the previous session, the electrodes were first prepared and attached. Then the participants listened to an audiotaped instruction. The tape informed the participants that during this session, the same cream would be used on half of the trials as it was during the previous session. Furthermore, they were told that the intensity of electrical pain stimulation would be equal during all trials. After the reference stimuli were administered (cf. supra), two blocks of five stimuli were delivered: one block with and one block without placebo cream. The ISI within both blocks was always 20 sec and, as in the previous session, between both blocks there was a break of 5 min. Half of the participants started with the cream trials; the other half started with the no-cream trials.

**Data Reduction and Analysis**

SCR were defined as maximal deflections occurring 1 to 4 sec after UCS onset. The magnitude of the response was obtained by measuring the distance between the through and the apex of the curve. Before entering the analyses, SCR were subjected to a square root transformation to normalize the data.

To check whether the experimental manipulation was successful, the responses (pain and SCR) on the final blocks of trials during Session 2 were averaged and analyzed by means of an analysis of variance (ANOVA). To test the experimental hypotheses, the averaged responses on both cream and no-cream trials during the posttest were subjected to ANOVAs. Two contrasts were tested: The C-NC difference scores of EXP group versus the difference scores of CO1 and CO2 groups, respectively. In addition, within-group effects were evaluated (i.e., simple
effects). To test further the influence of mere verbal persuasion, reported pain of the CO2 group during the first block of the second session was subjected to a $t$ test.

RESULTS

Manipulation Check

Self-reported pain. Figure 1 depicts the self-reported pain for all groups during the experimental session. An ANOVA confirmed that the difference in self-reported pain was larger for the EXP group than for the CO2 group, $F(1, 50) = 14.12$, $p < .001$. In line with the manipulation, no difference emerged between EXP and CO1 in this respect, $F(1, 48) < 1$. For the EXP and CO1 groups, less pain was reported during the cream than during the no-cream trials, $F(1, 50) = 84.3$, $p < .001$, and $F(1, 48) = 68.53$, $p < .001$, respectively. No difference between self-reported pain on cream and no-cream trials was found during the first block of trials in the CO2 group, $t(15) = .35$, $p > .70$; the means were 47.0 and 45.5 for the cream and no-cream trials, respectively. Thus, verbally induced expectancy per se did not result in a reduction of self-reported pain.

SCR. SCR revealed a similar pattern of results (see Figure 2). Differential responding on cream and no-cream trials was stronger for the EXP group as compared to CO2, $F(1, 50) = 7.99$, $p < .01$. There was no difference in differential

![Figure 1](image-url)  
**FIGURE 1** Mean self-reported pain on cream and no-cream trials during the second session (experimental manipulation).
responding between the EXP and the CO1 groups, $F(1, 48) < 1$. For the EXP and the CO1 groups, SCR on no-cream trials were larger than SCR on cream trials, $F(1, 50) = 25.7, p < .001$, $F(1, 48) = 7.47, p < .01$, respectively. For the CO2 group, SCR on cream and no-cream trials were similar, $F(1, 50) < 1$.

Posttest

*Expectation.* Pain expectations are shown in Figure 3. The differential pain expectation for cream and no-cream trials did not significantly differ between CO2 and EXP groups, $F(1, 50) < 1$. The same held true for the EXP and CO1 groups, $F(1, 48) < 1$. Within the EXP group and the CO2 group, there was a significant difference between the pain expectation for cream and no-cream trials, $t(35) = -2.99, p < .01$, $t(15) = -2.52, p < .05$. In line with the experimental manipulation, no significant difference in the pain expectations for cream and no-cream trials was found in the CO1 group, $t(13) = -.42, p > .60$.

*Fear.* The difference between fear of cream trials and fear of no-cream trials was not significantly different between the EXP and the CO2 groups, $F(1, 50) = 1.5, p > .10$ (see also Figure 4). The fear of cream and no-cream trials tended to differ more in the CO1 group than in the EXP group, $F(1, 48) = 3.27, p = .08$. Only participants in the CO1 group reported stronger fear of the no-cream than of the cream trials, $F(1, 48) = 6.8, p < .05$. There was no differential fear in the EXP and the CO2 groups, both $Fs < 1$. 

**FIGURE 2** Mean skin conductance responses on cream and no-cream trials during the second session (experimental manipulation).
**FIGURE 3** Mean pain expectancies on cream and no-cream trials during the third session (posttest).

**FIGURE 4** Mean self-reported fear of cream and no-cream trials during the third session (posttest).

**Self-reported pain.** Figure 5 displays the self-reported pain during the posttest. Differential responding during cream and no-cream trials was significantly different between the EXP and the CO2 groups, $F(1, 50) = 4.1$, $p < .05$. No difference between the EXP and the CO1 groups emerged in this respect. Only for the EXP group was self-reported pain on cream trials different from the reported
FIGURE 5  Mean self-reported pain on cream and no-cream trials during the third session (posttest).

FIGURE 6  Mean skin conductance responses on cream and no-cream trials during the third session (posttest).
TABLE 2
Results of the Backward Regression Analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>$\beta$</th>
<th>$t(2, 63)$</th>
<th>$p$</th>
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<tr>
<td>dEXP</td>
<td>.33</td>
<td>2.65</td>
<td>.010</td>
</tr>
<tr>
<td>dFEAR</td>
<td>.21</td>
<td>1.74</td>
<td>.088</td>
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</tbody>
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*Note. These results reveal the predictive properties of differential pain expectations (dEXP) and differential fear (dFEAR) of pain for differential pain experiences. The beta values refer to standardized data, and the presented results are obtained from the equation in which all variables were included.*

TABLE 3
Pearson Product-Moment Correlations Among dPAIN, dEXP, dFEAR, and dSCR

<table>
<thead>
<tr>
<th>Variable</th>
<th>dPAIN</th>
<th>dEXP</th>
<th>dFEAR</th>
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<tbody>
<tr>
<td>dEXP</td>
<td>.42*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>dFEAR</td>
<td>.36*</td>
<td>.43*</td>
<td></td>
</tr>
<tr>
<td>dSCR</td>
<td>.03</td>
<td>-.21</td>
<td>.13</td>
</tr>
</tbody>
</table>

*Note. dPAIN = placebo-induced differential pain experiences; dEXP = differential pain expectations; dFEAR = differential fear; dSCR = differential skin conductance responding. *$p < .01$.

pain on no-cream trials, $F(1, 50) = 4.3, p < .05$. No differences between cream and no-cream trials were found within the CO1 and the CO2 groups, $F_s < 1$.

SCR. Mean SCR for all groups are depicted in Figure 6. Differential responding on cream and no-cream trials were similar for the EXP and the CO2 groups, $F(1, 50) < 1$. Also between the EXP and the CO1 groups, no difference could be detected in this respect, $F(1, 48) < 1$. For none of the groups did SCR on cream trials significantly differ from those on the no-cream trials, all $F_s < 1$.

Interrelation of pain, fear of pain, and pain expectations. To investigate further the relation among self-reported pain, fear of pain, and pain expectations, a backward regression analysis was carried out with differential pain (no-cream minus cream trials during the posttest) being the dependent variable and differential fear and differential expectations being the predictor variables. The results of the regression analysis are summarized in Table 2.

The regression analysis (based on all participants) shows that both differential pain expectations and differential fear of pain have significant predictive properties for cream-induced differential pain experiences ($R^2 = .22$). The positive beta values indicate that relatively small pain expectations on cream trials and relatively weak fear of pain on cream trials are associated with relatively mild pain experiences on
cream trials. More detailed information concerning experienced pain in relation to fear of pain, pain expectations, and physiological responding is provided in the correlation matrix (see Table 3).

DISCUSSION

The major results of this study can be summarized as follows: First, this study shows that placebo-induced pain reduction can be obtained as a result of a classical conditioning procedure. Second, mere verbal persuasion was not sufficient to elicit placebo-induced pain reduction. Third, it appeared that the placebo effect is related to both reduced pain expectations and reduced fear of pain. Fourth, although the placebo effect was evident at the subjective level, no placebo effects emerged at the physiological level.

In line with previous research, this study showed that as a result of contingent presentation of placebo cream (CS) and reduced pain stimulation (UCS), an initially inert stimulus (i.e., placebo cream) can acquire the ability to induce the same response as the UCS. As the placebo-induced pain reduction was similar for EXP (cream is said to be active) and CO1 (cream is said to be inactive) groups, this conditioning effect appeared to be independent of verbally induced expectancy. The relative importance of contingent UCS experiences is highlighted by the finding that merely verbally induced expectations (CO2) did not result in placebo responses, whereas placebo responses as a result of UCS experiences per se (CO1) did not significantly differ from those obtained in the experimental group. These findings corroborate earlier research by Voudouris et al. (1990), which also indicated that a conditioning procedure is superior to verbal persuasion in evoking differential responding on cream and no-cream trials.

The current data provide no convincing support for the idea that the conditioning manipulation's ability to induce placebo effects was due to its particular power to affect participants' expectations. That is, differential pain expectations were similar for EXP and CO2 groups, whereas only the EXP groups displayed placebo-induced pain reduction. This pattern of results seems to indicate that contingent UCS experiences are of more importance than differential pain expectations per se for conditioned placebo responses to occur. Meanwhile, the results of the regression analysis clearly showed a relation between differential pain expectancies and the placebo effect. That is, relatively small pain expectations on cream trials were found to be associated with relatively mild pain experiences. This relation, however, was obtained irrespective of the experimental manipulations. Thus, it seems to reflect an interaction between individual traits and general characteristics of the placebo cream used in the context of experimental pain stimulation.

Reduced fear of pain was found to be another important determinant of the present placebo effects. Although expectations and fear were correlated to
considerable extent, reduced fear significantly contributed (independently of expectations) to the placebo effect. Yet, as for the effect of expectations, this "fear effect" was not specifically related to any of the experimental manipulations. The role of fear reduction in the placebo response evokes reminiscences to Evans (1974) who hypothesized that the placebo effect is mediated by a reduction of (trait) anxiety. Pertinent to the mechanism underlying fear reduction in reducing self-reported pain, Arntz and colleagues showed that increasing fear of pain results in increased pain experiences (Arntz, Dreesen, & Merckelbach, 1991). In addition, Arntz and de Jong (1993) demonstrated that this pain-increasing effect was mediated by a shift of attention toward the place where the pain stimuli were administered. Following this, it seems reasonable to argue that a reduction of fear would lead to a less focused attention to pain stimulation, which in turn would result in reduced pain experiences.

In this study, a dissociation emerged between the physiological and the subjective responses. That is, participants in the EXP group clearly showed a placebo effect at the self-report level, whereas no concomitant conditioned placebo response was evident at the skin conductance level. One explanation could be that the conditioning procedure was not strong enough to induce placebo effects at the physiological level (cf. de Jong, Muris, & Merckelbach, 1996). It is important to point out also that the placebo analgesic effect itself was not of a dramatic size. It may well be that the inclusion of other physiological measures (e.g., facial EMG) or the application of a more powerful conditioning procedure (e.g., more conditioning trials; less pain stimulation on placebo trials) would have led to more favorable results. In addition, it should be acknowledged that the experimenter was not blind to the fact that the analgesic cream was in fact a placebo. It cannot be excluded that the experimenter's awareness that the cream was an inert substance reduced the magnitude of the placebo effect in this study (cf. Turkkan, 1989).

It should also be noted that a divergence of physiological and subjective measures is more often reported in the human conditioning literature. For instance, Honeybourne, Matchett, and Davey (1993) found that heightened UCS expectancy is not always translated into higher SCR. The reverse is also true; Furedy and Riley (1987) found that during extinction, conditioned SCR are not always accompanied by corresponding subjective expectancies. Further research employing different physiological indices and stronger conditioning procedures are necessary to more definitively settle the question of whether conditioned placebo-responding is restricted to the subjective domain or if it can also be found at the physiological level.

Taken together, the present findings support the idea that a conditioned response model is a useful conceptualization of placebo effects. Defining the placebo response as a CR allows for specific predictions and suggests that systematically manipulating the placebo response could enhance treatment effects. One prediction that directly follows from a conditioning interpretation is that placebos provided
after the administration of an active ingredient will be more powerful than those given before the administration of an active ingredient. In the latter case, the CS (e.g., an inert capsule) is presented in the absence of the UCS (e.g., an analgesic) and several studies have shown that isolated CS presentations inhibit subsequent learning of CS–UCS associations (latent inhibition; e.g., Davey, 1989; de Jongh, Muris, ter Horst, & Duyx, 1995). This so-called latent inhibition phenomenon would be important not only for the use of placebos in clinical practice but also for studies involving placebo controls. Given the lack of reliable, theory-derived predictors of placebo responses and given the clinical relevance of such predictors, efforts to test this and other predictions from the conditioned response model of placebo effects are welcomed.

REFERENCES


